

Amendments to the Specification

Please insert the following new paragraph on page 1 at the next line below the Title:

This application is a national stage application under 35 U.S.C. § 371 from PCT Application No. PCT/US2003/030607, filed September 25, 2003, which claims the priority benefit of U.S. Provisional Patent Application No. 60/413,409, filed September 25, 2002.

Please replace the paragraph beginning on page 3, line 21 of the specification with the following amended paragraph:

Figure 8 shows that caspase inhibitors do not enhance the cytotoxic effects of BCNU on normal astrocytes. Cells were plated (1000 cells/well) on 24-well coverslips and exposed to BCNU (40 µg/ml for 1 hour) alone or to BCNU in combination with caspase inhibitors (CI-8 and CI-9). Cells were exposed to caspase inhibitors for 24 hours at a concentration of 20µM each. After a 48 hour recovery period, cells were MTT/DAPI-stained to determine viability. Error bars represent s.e.m. Astrocytes were killed by BCNU but not by inhibitor of caspase-8. While inhibition of caspase-8 did not rescue these cells, neither did it make them worse than BCNU alone. The failure to rescue is consistent with ideas that BCNU might preferentially work through activation of caspase-9. In support of this, inhibition of caspase-9 actually conferred partial protection on astrocytes.

Please replace the paragraph beginning on page 4, line 1 of the specification with the following amended paragraph:

Figure 9 shows that co-application of a caspase inhibitor with an anti-oxidant is more effective at killing tumor (UT-12 glioblastoma) cells than application of the caspase inhibitor by itself. Cells were plated (1000 cells/well) on 24-well coverslips and exposed to caspase 9 inhibitor (20 µM) ± Vitamin C (20 µg/ml) for 24 hours. After a 48 hour recovery period, cells were MTT/DAPI-stained to determine viability. Error bars represent s.e.m.

Please replace the paragraph beginning on page 4, line 4 of the specification with the following amended paragraph:

Figures 10A-F show ~~Figure 10 shows~~ that application of caspase inhibitors to SW480 colon cancer cells not only fails to rescue from cisplatin-induced death, but actually decreases the number of cells still further from the reduction obtained with cisplatin alone. The figures

show DAPI-staining of SW480 cells after 24 hour treatment with caspase-inhibitors ± cisplatin, thus revealing the cellular nuclei. Figure 10A: Control; Figure 10B, pan-inhibitor; Figure 10C, caspase-3 inhibitor; Figure 10D, cisplatin; Figure 10E, cisplatin + pan-inhibitor; and Figure 10F, cisplatin + caspase-3 inhibitor. The caspase inhibitors and cisplatin were added at a concentration of 20 µM.